In the Specification:

Please amend the specification as shown:

Please delete the paragraph on page ~~2~~ 3, lines ~~16-26~~ 4-14 and replace it with the following paragraph:

The dinucleotide binding fold and the GG motif are found e.g. within the N-terminal domain of FAD containing enzymes (e.g. reductases, dehydrogenases, hydroxylases, peroxidases, and oxidases). FAD containing enzymes can be classified into five groups GR1, GR2, FR, PCMH, and PO according to the sequences of their FAD binding domains and additional conserved sequence motifs (Dym and Eisenberg, Protein Science, 10:1712-1728, 2001). The consensus sequence of GR1 and GR2 is GxGxxG. The GG motif RhGGRhxxT/S **(SEQ ID NO: 76)** is commonly found in oxidases, e.g. L-amino acid oxidases, monoamino oxidases, polyamine oxidases, and putrescine oxidases, wherein x describes any amino acid, and h describes a hydrophobic amino acid.

CD

4.14.08

Please delete the paragraph on page ~~3~~ 8, lines ~~20-23~~ 1-4 and replace it with the following paragraph:

Analysis of the sequences SEQ ID NO: 2, 4, and 6 revealed that APIT comprises a sequence similar to known dinucleotide binding folds which are characteristic for flavoproteins (Fig. 4c). The GG-motif (consensus sequence RhGGRhxT/S) **(SEQ ID NO: 76)** is found adjacent to the dinucleotide binding fold.

Please delete the paragraph on page ~~7~~ 11, line ~~28~~ 12 to page ~~8~~ 12, line ~~3~~ 4 and replace it with the following paragraph:

A further aspect of the present invention is a nucleic acid coding for the polypeptide as described above. The total mRNA of the mantle gland, the nidamental gland, the digestive gland, and the opaline gland can be prepared by standard methods. The mRNA can be reverse

transcribed using the tagged oligo dT oligonucleotide (Oligo 1, Fig. 4b). The tag is a random sequence not expected to be present within Aplysia mRNA to be reverse transcribed. PCR can be performed using the degenerated primer (Oligo 2) derived from the APIT peptide VFEYSDR **(SEQ ID NO: 48)** and the specific primer (Oligo 3) directed against the tag sequence of the oligo dT primer Oligo 1. The amplified sequence can be cloned into a standard vector and can be sequenced by standard techniques. By this strategy, the 3' terminal sequence of the APIT gene can be obtained. The 5' terminal sequence can be obtained by the RACE strategy. The mRNA from selected tissues (see above) is reverse transcribed using an oligonucleotide derived from the known 3' terminal sequence (e.g. Oligo 4, or Oligo 6) and can be treated with a terminal transferase in the presence of CTP, resulting in a 3'-poly-C-sequence (at the minus strand). PCR can be performed using a tagged primer against the poly-C-sequence (Oligo 5) and a specific primer, e.g. Oligo 4, or Oligo 6. The amplified product can be cloned and sequenced by standard techniques. Finally, for obtaining full-length cDNA clones, specific primers, e.g. Oligo 8 and Oligo 9 can be used. By this strategy, three different clones were obtained and sequenced. The nucleotide sequences are described in SEQ. ID. No.1, 3, and 5 which are identical to 97% (1560 of 1608) of the nucleotides. 42 of 48 mutations are silent mutations which have no effect upon the amino acid sequence.

QA

4.14.08

Please delete the paragraph on page ~~20~~ 31, lines ~~24-36~~ 29 to pg 32 line 10 and replace it with the following paragraph:

A, N-terminal **(SEQ ID NO: 33)** and internal peptide sequences **(SEQ ID NOS 47,49-50, 77, 51, 37, and 52-55 disclosed respectively in order of appearance)** of the APIT protein.

B, List of oligonucleotides used for cloning of the APIT gene **(SEQ ID NOS 58-61, 63, 62, and 64-66 disclosed respectively in order of appearance)**.

C, Nucleotide sequence of the APIT CDNA **(SEQ ID NO: 1)** and the derived amino acid sequence **(SEQ ID NO: 2)**. The dinucleotide binding fold (VAVVGAGPGGANSAYMLRDSG-LDIAVFE) **(SEQ ID NO: 56)** and the GG-motif

(RVGGRLFT) **(SEQ ID NO: 57)** are indicated by boxes. Consensus amino acid residues are indicated by bold letters. The N-terminal sequence of mature APIT (dashed line) and of internal peptides (solid line) derived by Edman degradation and mass finger prints are indicated. Sequence variations of the three clones are indicated by small boxes **(SEQ ID NOS 3 and 5 are also disclosed respectively in order of appearance)**.

D, Variation of the N-terminus of APIT in 11 further clones **(SEQ ID NO: 78)**.

CS 4.14.08

Please delete the paragraph on page ~~26~~ 41, line ~~28~~ 15 to page ~~27~~ 42, line ~~3~~ 7 and replace it with the following paragraph:

Cloning of the APIT gene. In order to dissect mantle gland, nidamental gland, digestive gland and opaline gland some animals were relaxized by injection of 5 '10 ml sterile $MgCl_2$ solution (380 mM). Isolated tissues were frozen immediately in liquid nitrogen. Total RNA was prepared from these tissues using the 'peq gold TRIfast' reagent (Peqlab). mRNA was reverse transcribed using the tagged oligo dT oligonucleotide 5'-tcc taa cgt agg tct aga cct gtt gca $t_{(18)}$-3' **(SEQ ID NO: 58)** (Fig. 4B, oligo 1) and the Superscript II polymerase (LIFE) at 42EC. In order to amplify a fragment of the APIT gene the degenerated primer 5'-tc gtg ttc gar tac tci gay cg-3' **(SEQ ID NO: 59)** derived from the APIT peptide VFEYSDR **SEQ ID NO: 48)** (Fig. 4B, oligo 2) and the specific primer 5'- ctg tag gtc tag acc tgt tgc a-3' **(SEQ ID NO: 60)** (Fig. 4B, oligo 3) directed against the tag sequence of the oligo dT-primer was used. PCR was performed with the expand long template system (ROCHE, Mannheim) at 68EC and the product was cloned into the pCMV-vector (Stratgene) and sequenced. The 5' terminal cDNA of APIT was cloned using the 5' RACE System (LIFE) according to the manufacturers instructions. Primers 5'-ccg tgt aga tct cac tgc cat a-3' **(SEQ ID NO: 61)** (Fig. 4B, oligo 4) or 5'-ccg ttg agt tgt aga cct-3 **(SEQ ID NO: 62)** (Fig. 4B, oligo 6) were combined with the primers 5'-ggc cac gcg tcg act agt acg ggi igg gii ggg iig-3' **(SEQ ID NO: 63)** (Fig. 4B, oligo 5) or 5'-aatt ggc cac gcg tcg act agt ac-3' **(SEQ ID NO: 64)** (Fig. 4B, oligo 7) to yield a product which was cloned into the pCDNA3-vector (Invitrogen) and sequenced. Finally, full length APIT cDNA was obtained by amplifying the APIT using the specific primers 5' ' aa ttc tcg tct gct gtg ctt ctc ct **(SEQ ID NO:**

65) (Fig. 4B, oligo 8) and 5' ' gac tta gag gaa gta gtc gtt ga (SEQ ID NO: 66) (Fig. 4B, oligo 9) and cloned into the pGEX-4T3 Vector (Amersham). DNA from 3 clones of transfected E.coli was prepared and sequenced.

Please delete the paragraph on page 33, line 34 to page 34, line 15 and replace it with the following paragraph:

Therefore, 20.000 HeLa cells/well were seeded in a 96 well plate one day prior to transfection. Transfection was performed with 0.25 ig siRNA directed against
Prx I having the sequence (SEQ ID NO: 9):
5'-GGCUGAUGAAGGCAUCUCGdTdT-3'
3'-dTdTCCGACUACUUCCGUAGAGC-5' (SEQ ID NO: 73),
Lamin A/C having the sequence (SEQ ID NO: 30):
5'-CUGGACUUCCAGAAGAACAdTdT
3'-dTdTGACCUGAAGGUCUUCUUGU-5' (SEQ ID NO: 74),
and Luciferase having the sequence (SEQ ID NO: 31):
5'-CUUACGCUGAGUACUUCGAdTdT-3'
3'-dTdTGAAUGCGACUCAUGAAGCU-5' (SEQ ID NO: 75),
as control and 2 il transmessenger per well using the transmessenger transfection kit (Qiagen, Hilden, Germany) according to manufacturers instructions. For APIT treatment (40ng/ml) transfections were conducted in triplicates. 24 h after transfection cells were splitted and grown for additional 48 h before fresh medium with or without APIT was added for 6h. Assay conditions which led to a 50 to 70 % reduction of the metabolic activity of treated cells were chosen for RNAi experiments. Metabolic activity was determined as described in Example 2. In parallel, RNA from about 50.000 cells was isolated using the RNeasy 96 BioRobot 8000 system (Qiagen) 48 h after transfection. The relative amount of mRNA was determined by realtime PCR using Quantitect™ SYBR Green RT-PCR Kit from Qiagen following manufacturers instructions. The expression level of Prx mRNA was normalised against the internal standard GAPDH. The following primers were used: Prx I 5': CTGTTATGCCAGATGGTCAG (SEQ ID NO: 67), Prx I 3': GATACCAAAGGAATGTTCATG (SEQ ID NO: 68),
Lamin A/C 5':CAAGAAGGAGGGTGACCTGA (SEQ ID NO: 69),